out for about 200 femtoseconds, which is a few vibrational periods of the I-C bond. We can get direct information on the potential energy surface, and that is very exciting." The potential energy surface is a profile of the energy that is holding the molecular components together, and it varies according to the separation between them. "This is what every chemist wants to know, because once you know the potential energy surface, you know everything about the system."

For the foray into the bimolecular reaction, Zewail joined forces with Richard Bernstein of the University of California, Los Angeles. One potential problem with dealing with bimolecular reactions in Zewail's system is that the normal time between intermolecular collisions is very long compared with the subsequent reaction time. Zewail got over this by exploiting the fact that, when hydrogen iodide and carbon dioxide pass through the molecular beam process, they form a loosely bound complex. The desired reaction was then initiated by pumping energy into the H-I bond, which then breaks, propelling the hydrogen atom forcefully in the direction of an oxygen of the carbon dioxide.

"The question is, when the hydrogen is attacking the carbon dioxide, how long does the dancing between them go on before a final product is formed," says Zewail. "The answer is, quite a long time, 5 picoseconds. There had been some indirect evidence for this, but, once again, we were able to view it in real time."

Zewail's femtosecond chemistry undoubtedly is a dramatic advance, but it goes beyond simply increasing the time resolution of watching reactions. "We all get excited when we step up time resolution by a factor of 10," he says, "but what is most important here is that all the molecular dynamics are frozen."

When you pump energy into a molecule for a picosecond (1000 femtoseconds), things begin to happen before the pulse is extinguished: the time scale for vibrations and rotations within the molecule are shorter than the time scale of the pulse. "But with a femtosecond pulse, nothing happens during the lifetime of the pulse—no vibrations, no rotations, nothing. You are looking at a frozen configuration, and after that you are free to follow in real time what happens to the chemistry." ■

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ADDITIONAL READING

M. Dantus *et al.*, "Real-time femtosecond probing of 'transition states' in chemical reactions," *J. Chem. Phys.* **87**, 2395 (1987).

N. F. Scherer *et al.*, "Real-time picosecond clocking of the collision complex in a bimolecular reaction," *ibid.*, p. 1451.

Gene Makeup a Surprise

A recent study shows that two blood proteins with very different functions have surprisingly similar gene sequences and structures. New data indicate that apolipoprotein(a), a plasma protein that may be a culprit in atherosclerosis and heart disease, bears a remarkable similarity to plasminogen, a precursor of the enzyme that dissolves blood clots. The genetic and physical similarity between two proteins, previously thought to be unrelated, is completely unexpected. Richard Lawn, John McLean, James Tomlinson, Dan Eaton, and their colleagues of Genentech in South San Francisco, and Angelo Scanu and Gunther Fless of the University of Chicago report the complimentary DNA sequence of apolipoprotein(a) and its protein organization in the 12 November issue of *Nature*.

Apolipoprotein(a) or apo(a) is the protein part of lipoprotein(a). The latter belongs to a still larger family of particles called low-density lipoproteins. "Lipoprotein particles transport cholesterol and other insoluble fatty substances through the blood," says Lawn. "Recently, numerous studies have shown a correlation between atherosclerosis, heart disease, and an increasing concentration of lipoprotein(a)." Lawn and his collaborators propose that the apo(a) portion of the lipoprotein(a) particle may somehow provoke hardening of the arteries or heart attacks.

The new results show that the internal structure of apo(a) contains an unusual series of repeated protein units or domains. They are particularly striking because of their number—37 in all for apo(a) in contrast to 5 such units for plasminogen. The gene structure that codes for this redundant arrangement in the apo(a) protein is also highly repetitive. "Apo(a) looks like a plasminogen gene gone awry," note the researchers in their report.

The repeated domains of both apo(a) and plasminogen proteins are called kringles because their twisted three-dimensional shapes look like a kind of Danish pastry. "Kringles contain binding sites for the molecule and orient it properly," says Lawn. For example, the kringles of plasminogen allow it to bind to fibrin, the protein that actually forms blood clots. This permits a separate region of the plasminogen protein to be activated by plasminogen activator to form the enzyme plasmin. Plasmin is the enyzyme that dissolves the clot.

The kringles of apo(a) are different, not only because there are many more of them, but also because they contain a large number of sugar residues. Although no one knows the function of the apo(a) protein, researchers believe that it somehow invites trouble.

Perhaps the makeup of apo(a) or its high carbohydrate content increases the overall ability of the lipoprotein(a) particle to penetrate cells, speculates Scanu. As a result, the cholesterol-carrying complex may penetrate the endothelial lining of an artery easily, he says. Once there, it may become entrapped and resist the normal degradation and removal processes. Then, cholesterol may have a greater chance to accumulate and form a fatty deposit or atherosclerotic plaque.

"I view this as a clinical problem, a practical problem," says Scanu. Researchers used to think that only certain people had lipoprotein(a) in their blood but now they recognize that everyone has at least some of it. However, no one is certain whether the amount of the lipoprotein(a) or the type of apo(a) that it contains presents the greater risk.

Scanu says that in all of the public recommendations made by the American Heart Association the risk of heart disease attributable to lipoprotein(a) is not mentioned. People inherit a certain form of apo(a) and cannot eliminate their risk solely on the basis of diet. This characteristic distinguishes lipoprotein(a) from other low-density lipoproteins, such as the B-100–containing lipoproteins that are affected by diet. Like lipoprotein(a), they also carry cholesterol around in the blood but are not thought to be dangerous unless they occur at very high levels.

The new findings should make it possible to devise methods for measuring the amount and type of apolipoprotein(a) and lipoprotein(a) in the blood, Scanu says. Then researchers can correlate this information with susceptibility for atherosclerosis and heart disease. In addition, the new results should make it possible to determine how apo(a) and lipoprotein(a) lead to atherosclerotic plaque formation. Armed with this information, researchers may then be able to design methods for interfering with these processes. ■ DEBORAH M. BARNES